Remarks

Claims 1-21 are pending in the application. Claims 1-9 and 16-21 are subject to examination, claims 10-15 having been withdrawn from consideration as being not drawn to the elected species. The elected species is a method of treating an inflammatory disorder of the epithelial tissue comprising the administration of (R)-tofisopam, wherein the compound is administered as a dose of less than about 50 mg/day.

Claims 1-9 and 16-21 stand rejected. Reconsideration is respectfully requested in view of the following remarks.

Response to Obviousness-type Double Patenting Rejection

Pat. 6,864,251

Without acquiescing in the rejection, a terminal disclaimer over claims 1-12 of the '251 patent is filed herewith.

Application 10/727,940

The present Office Action, while reciting an obviousness-type double patenting rejection over the '251 patent, also refers to "the '940 application", without making a formal rejection. To the extent Examiner means to refer to application 10/727,940 in the remarks regarding "the '940 application" as a separate rejection, it should be noted that the '940 application has been abandoned.

Response to Section 102 Rejection

Claims 1-6 and 16-21 have been rejected as anticipated by Ito, Chihiro, et al., "Pharmacological Studies of Tofisopam," *Res. Lab Pharmacol.*, Mochida Pharm. Co., Ltd., Tokyo, Japan (1981). The rejection alleges that Ito teaches the pharmacological effects of tofisopam, both *in vivo* and *in vitro*, to include elevation in pain thresholds when administered orally. The rejection also alleges that the claims of the present application suggest the same compound as Ito, and that "whatever characteristics the drugs have in the references necessarily flows to the claimed invention." *See present Office Action at p.5, first full paragraph.*

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Vendegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Applicant notes again that none of the biological effects of tofisopam reported by Ito indicate treatment of an inflammatory disorder of epithelial tissue. While Examiner again makes specific reference to the elevation of pain thresholds, Applicant reiterates that there is nothing in the disclosure of Ito that teaches or suggests any relation of the observed increase in pain threshold to any effect involving inflammation, let alone an inflammatory disorder of the epithelium. Therefore, Examiner has made no assertion that any portion of Ito expressly anticipates the claims of the present application.

Furthermore, Ito does not inherently anticipate the claimed invention. To establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co. v. Monsanto Co.*, 20 USPQ2d 1746, 1749 (Fed.Cir. 1991). Thus, "anticipation by inherent disclosure is appropriate only when the reference discloses prior art that must *necessarily* include the unstated limitation, [or the reference] cannot inherently anticipate the claims." *Transclean Corp. v. Bridgewood Servs., Inc.*, 62 USPQ2d 1865, 1871 (Fed. Cir. 2002) (emphasis in original).

It is not sufficient if a material element or limitation is "merely probably or possibly present" in the prior art. *Trintec Indus., Inc. v. Top-U.S.A. Corp.*, 63 USPQ2d 1597, 1601 (Fed. Cir. 2002). As the CCPA stated in *In re Oelrich*, 212 USPQ 323, 326 (CCPA 1981) (quoting *Hansgirg v. Kemmer*, 40 USPQ 665, 667 (CCPA 1939)) (internal citations omitted):

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.

See also, *Mehl/Biophile International Corp. v. Milgraum*, 52 USPQ2d 1303, 1305-06 (Fed. Cir. 1999); *In re Robertson*, 49 USPQ2d 1949, 1951 (Fed. Cir. 1999).

"In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the alleged inherent

characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd.Pat.App. & Int.1990). Examiner has not, and cannot, make such a showing.

In the present rejection, Examiner has seemingly confused ***what must necessarily flow from the teachings of the applied art*** with ***what characteristics of the drug necessarily flow with the drug itself.*** Examiner's position that "whatever characteristics the drugs have in the references necessarily flows to the claimed invention" has no basis in fact other than the drug used in the presently claimed method of treatment appears to be similar to the drug disclosed in Ito. If "similarity of the drug" was enough basis in fact to support inherent anticipation of a method of treatment, then **all** applications claiming a method of treating anything by a known drug would be deemed unpatentable. No such interpretation is predicated by any current case law. The mere fact that it is possible that oral administration of tofisopam for elevating pain thresholds as disclosed by Ito ***might also*** result in alleviating an ***undisclosed*** inflammatory disorder of the epithelium is not sufficient to establish anticipation. *See Mehl/Biophile International, supra* (claimed method of laser removal of hair by aligning laser over follicles not inherently anticipated by reference teaching laser removal of tattoos; mere possibility of such an alignment occurring during laser tattoo removal does not suffice to show anticipation). *See also, Perricone v. Medicis Pharmaceutical Corp.*, 77 U.S.P.Q.2d 1321 (Fed. Cir. 2005) (Disclosed use of Pereira's lotion, i.e., topical application, does not suggest application of Pereira's lotion *to skin sunburn.*) emphasis added.

What necessarily flows from the teachings of the applied art is what may be inherently understood by one skilled in the art ***from what is disclosed in the reference***, not the latent and/or undiscovered physical characteristics or physiological effects of the drug itself. There is nothing in the disclosure of Ito that teaches or suggests the use of tofisopam for the treatment of an inflammatory disorder of the epithelium. There is nothing in the disclosure of Ito that relates the observed increase in pain threshold to any effect involving inflammation, let alone an inflammatory disorder of the epithelium. Further still, no dose information is even provided by Ito, let alone the limitation of a method of treatment wherein a compound is administered at a dose of less than 50 mg/day. A mere possibility of such result, or even a probability of that

result, is insufficient to give rise to anticipation. *Trintec Indus., supra.* Only a result that *inevitably* flows from the teaching of a reference may inherently anticipate. To suggest that administration of tofisopam at a dose of less than 50 mg/day for the treatment of an inflammatory disorder of the epithelium ***necessarily*** flows from the mere disclosure of an elevation in pain thresholds when tofisopam is administered orally at an unspecified dose, would be unprecedented. Therefore, Ito fails to disclose each and every element as set forth in independent Claim 1. Thus, Claim 1, and its dependent claims, are not and cannot be anticipated by Ito.

As explained previously, the claims of the present application are further distinguished from Ito with respect to the administrated dose. Claim 1 of the present application defines a method of treatment wherein a compound is administered at a dose of less than 50 mg/day. No dose information is given by Ito. Therefore, Ito fails to disclose each and every element as set forth in Claim 1. Thus, Claim 1, and its dependent claims, are not anticipated by Ito. Applicant also notes that the present rejection does not seem to acknowledge this limitation of dose, and therefore requests identification of where support from the cited references may be found, should Examiner continue to uphold the present rejection.

While the present rejection applies to Claims 1-6 and 16-21, only the limitations of independent Claim 1 are addressed. Applicant notes again that the dependent claims recite additional features that further distinguish over Ito. Ito fails to disclose a dosage of less than about 25 mg/day (Claim 2), less than about 10 mg/day (Claim 3), less than about 1 mg/day (Claim 4), less than about 25 mg/ml (Claim 5), and less than about 1 mg/ml (Claim 6). Ito fails to disclose treatment of an inflammatory disorder of the epithelium which is a skin disorder (Claim 7). Ito fails to disclose treatment of an inflammatory disorder of the epithelium which is a gastrointestinal disorder (Claim 8). Ito fails to disclose intracolonic or topical administration (Claim 9). Claim 16 is directed to a method wherein a compound which comprises at least 80% of the relevant (R)-enantiomer is administered. Claim 16 thus further distinguishes over Ito, which discloses only the racemate of tofisopam. The same as true of Claims 17-21, which are directed to administration of (R)-enantiomers.

Accordingly, Claims 1-9 and 16-21 are not anticipated by Ito. Reconsideration and withdrawal of the rejection is respectfully requested.

Conclusion

The claims remaining in the application are believed to be in condition for allowance. An early action toward that end is earnestly solicited.

Respectfully submitted,

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